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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/813,950	03/03/1997	MANFRED ASSMUS	583-252-0-FW	4092

22850 7590 02/11/2004

OBLON, SPIVAK, MCCLELLAND, MAIER & NEUSTADT, P.C.
1940 DUKE STREET
ALEXANDRIA, VA 22314

EXAMINER	
SELLERS, ROBERT E	
ART UNIT	**PAPER NUMBER**
1712	

DATE MAILED: 02/11/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	08/813,950	ASSMUS ET AL.	
	Examiner	Art Unit	
	Robert Sellers	1712	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 02 February 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☐ The period for reply expires _____months from the mailing date of the final rejection.

b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☐ The proposed amendment(s) will not be entered because:

   (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

   (b) ☐ they raise the issue of new matter (see Note below);

   (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____.

3. ☐ Applicant's reply has overcome the following rejection(s): _____.

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See the attachment*.

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☐ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: _____.

   Claim(s) objected to: _____.

   Claim(s) rejected: _____.

   Claim(s) withdrawn from consideration: _____.

8. ☐ The drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10. ☐ Other: _____

Robert Sellers
Primary Examiner
Art Unit: 1712

Claim 29 confining the amount of glycerol monostearate to from 33.3-50 wt.% based on 100% by weight of thermoplastic acrylic plastic A and glycerol monostearate B was inadvertently omitted from the rejections.

The Finality of the rejections in the Office action mailed December 1, 2003 is proper since the same rejections were applied in the non-Final Office action mailed October 15, 2003.

The 35 U.S.C. 103(a) rejection over Deleuil et al. is withdrawn since the claimed amount of from 25-50 wt.% of glycerol monostearate is based on 100% by weight of thermoplastic acrylic A and glycerol monostearate B (claim 25, lines 6-7) which is not recited.

The deficiencies in the first and supplemental Assmus declarations remain pertinent to the instant rejections for the reasons espoused on pages 2-3 of the Final rejection.

The claims are directed to a medicinal composition prepared by a method of hot-melt application of a thermoplastic coating and binder to the medicinal composition, thereby constituting a product-by-process claim.

"If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process (*In re Thorpe*, 227 USPQ 964, 966, Federal Circuit 1985 and MPEP § 2113, the "Product-by-Process Claims' section)." "Once the examiner provides a rationale tending to show that the claimed product appears to be the same or similar to that of the prior art, although produced by a different process, the burden shifts to applicant to come forward with evidence establishing an unobvious difference between the claimed product and the prior art product (*In re Marosi*, 218 USPQ 289, 292, Federal Circuit 1983 and MPEP § 2113, the section entitled 'Once a Product Appearing to be Substantially Identical is Found and a 35 U.S.C. 102/103 Rejection Made, the Burden Shifts to the Applicant to Show an Unobvious Difference')."

Based on the equivalent medicinal compositions of the applied prior art and claims containing equivalent Eudragit acrylic plastics and glycerol monosterate within the claimed proportions, the claimed product is obvious for the reasons espoused hereinbelow and in the previous Office actions.

The Assmus declarations do not establish an unobvious difference between the claimed and prior art product as indicated hereinabove and in the previous Final rejection.

The Petereit et al. article designates glyceryl monostearate as an excipient in paragraph 2.1.2 on page 2 (the last two lines). The teachings of a reference are not confined to the examples. Page 7, lines 3-10 states that

> " . . . an amount of less than 20% of excipients will result in a strong increase of initial dose, caused by damage of coatings on the particles [4]. Obviously the amount of excipient must be so high that a separating layer is formed also around the surfaces of the coated particles to prevent adhesion or even confluence of the coatings."

This disclosure combined with the 50% maximum set forth in the references instructs one skilled in the art to employ the glyceryl monostearate excipient of the Petereit et al. article in an amount of from 20-50% in order to control the initial dosage and prevent the adhesion and confluence of the coatings.

It is conceded that the content of glycerol monostearate in Example 4 (col. 5) of Yajima et al. 5,707,646 is 600 g/700 g of glycerol monostearate + Eudragit® E = 85.7% by weight. The complex of Yajima et al. comprises from 1-60% by weight of polymer, a low melting point substance (e.g. glycerol monostearate), from 10-70% by weight of sugar alcohol and from 0.1-7% by weight of basic oxide (col. 2, lines 45-51). Based on the minimum levels of the components, the maximum proportion of glycerol monostearate is 100% - (1% + 10% + 0.1%) = 88.9%.
The minimum proportion considering significant figures is 0.1% since the low melting point substance is required to be present. Thus, the concentration of glycerol monostearate based on 100% by weight of polymer is from 0.2% (0.1 ÷ 60.1 total) to 88.9% which embraces the claimed range of from 20-50% by weight.

The claims drawn to a medicinal composition containing a pharmaceutical active substance and thermoplastic coating and binder is addressed by the medicinal composition of Burguiere et al. 5,603,957 obtained from 60-85% by weight (col. 5, line 56) of film-forming polymer (P_1) such as Eudragit® RL and/or RS (col. 6, lines 7-10) and from 2-20% by weight of the composition of a plasticizer such as a stearate of glycerol (col. 6, line 35) which converts to from 2.2-25% of glycerol stearate based on 100% by weight of Eudragit® and glycerol monostearate.
The claimed glass transition temperature (Tg) of the mixture of at most 20°K below the Tg of thermoplastic acrylic A is inherent in the formulation of Burguiere et al. considering the equivalent types and amounts of thermoplastic acrylics and glycerol monostearate.

The claimed process of the product-by-process does not distinguish the claimed composition from that of Burguiere et al. for the reasons espoused hereinabove. Even if, arguendo, the method limitations are considered, Mueller et al. 5,552,159 sets forth the melt extrusion at preferably from 60°C-150°C (col. 3, lines 16-19) of an acrylic polymer (col. 2, lines 1-4) and a plasticizer (col. 3, line 6). Mueller et al. is applied as a secondary reference and need not recite every limitation of the claims. The primary reference to Burguiere et al. establishes the efficacy of utilizing a particular acrylic polymer such as Eudragit® RL and/or RS, and a certain plasticizer such as glycerol stearate.

Staniforth et al. 5,858,412 clearly names Eudragit® RS and RL polymers (col. 20, lines 29-31) and glycerol monostearate (col. 11, line 33). According to MPEP § 2131.02 (the section entitled "A Reference that Clearly Names the Claimed Species Anticipates the Claim No Matter How Many Other Species are Named"), "the comprehensiveness of the listing did not negate the fact that the compound claimed was specifically taught (*In re Sivaramakrishnan*, 213 USPQ 441, CCPA 1982)."

The equivalent combination of Eudragit® E and glycerol monostearate with the microcrystalline cellulose of Staniforth et al. inherently possess the claimed Tg of the mixture of at most 20°K below the Tg of thermoplastic acrylic A. The microcrystalline cellulose (col. 5, lines 51-54) diluent of Staniforth et al. is not precluded from the claimed composition which encompass dispersants (page 15, line 26 of the specification).

Neither Japanese Patent No. 51-91317 nor Rudnic et al. 5,484,608 recites the claimed glycerol monostearate content, although there is no restriction as to its quantity. It would have been obvious to employ the glycerol monostearate of the Japanese patent and Rudnic et al. and Pollinger et al. 5,695,784 within the proportion range of from 25-50% by weight of Petereit et al. in order to facilitate tablet disintegration, and as much as the 20% by weight of Burguiere et al. in order to optimize the flow properties characteristic of plasticizers.

The disclosure of deleterious results using Eudragit® E 12.5 polymer does not negate the suitability of Eudragit® RL 30D (col. 5, line 3) which is a species of the genus designated on page 11, line 8 of the instant specification.

The Japanese patent, Rudnic et al. and Pollinger et al. clearly name Eudragit® E and glycerol monostearate. The motivation to utilize the glycerol monostearate of these references in the amounts within the realm of Petereit et al. and Burguiere et al. are declaratively espoused in the latter patents. The teachings of a reference cannot be mitigated due to other embodiments or preferred permutations. The burden of proof is incumbent upon applicants to establish the non-obviousness of the claimed composition over the closest prior art formulations of the Japanese patent, Rudnic et al. and Pollinger et al. Such a burden has not been met by the evidence in the instant specification nor the declarations for the reasons present hereinabove.

Mueller et al. (col. 3, line 6) discloses the inclusion of plasticizers. Petereit et al. 5,292,522 (col. 3, lines 46-51 and col. 3, line 29) designates glycerol monostearate as a lipophilic emulsifier which prevents "agglutination of the pharmaceutical dosage forms during the coating process," thereby describing a flow-affecting property characteristic of plasticizers. Burguiere et al. sets forth as much as 20% by weight of glycerol monosterate as a plasticizer. It would have been obvious to employ the glycerol monostearate of Petereit et al. and Burguiere et al. as the plasticizer of Mueller et al. in order to optimize the flow properties.

The blend of acrylic polymer and plasticizer of Mueller et al. wherein the plasticizer is the glycerol monostearate of Petereit et al. and Burguiere et al. is equivalent to the claimed composition. Therefore, the composition of Mueller et al. inherently possess the claimed Tg of the mixture of at most 20°K below the Tg of thermoplastic acrylic A. Mueller et al. espouses the melt extrusion at preferably from 60°C-150°C (col. 3, lines 16-19) which is germane to the product-by-process limitations of the claims.

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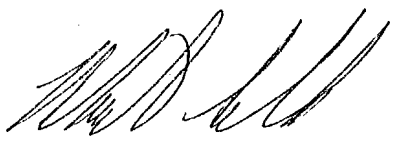

ROBERT E.L. SELLERS
PRIMARY EXAMINER